

U.S. Patent Application Serial No. **10/822,860**  
Response filed August 15, 2007  
Reply to OA dated May 17, 2007

**REMARKS**

Claims 1-14 are pending in this application, with claims 6-12 withdrawn from consideration. No amendment is proposed in this Response. It is believed that this Response is fully responsive to the Office Action dated **May 17, 2007**.

**Regarding the Office action summary.**

The Office Action Summary states that claims 1-5, 13 and 14 are rejected. However, based on the text of the Office action, it appears that claims 1, 2, 4 and 5 are rejected (Office action paragraph no. 9) and claims 3, 13 and 14 are objected to (Office action paragraph no. 10).

**The title of the invention is not descriptive.** (Office action paragraph no. 6)

The objection to the title is respectfully traversed.

The Examiner explains that the previous objection to the title was based on the Restriction requirement, and states that since the restriction requirement is now final, a new title is suggested.

However, Applicant notes that the restriction requirement was traversed, and the withdrawn claims are still pending. Applicant retains the right to petition for withdrawal of the restriction requirement, and therefore does not amend the title at this time.

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**Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Kretzschmar et al. (Genes & Development, 1999, 13:804-816, IDS item), in further view of Souchelnytokyi et al. (US Patent 6,103,869), and further in view of Harlow and Lane (Antibodies, a Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988, p. 93-94 and p. 142, previously cited). (Office Action paragraph no. 9)**

The rejection of claims 1, 2, 4 and 5 is respectfully traversed.

The polyclonal antibody of the present invention is characterized in that does not recognize the phosphorylation of the C-terminal region, but recognizes the phosphorylation of the linker region. (That is, the recitation "**specific** for a phosphorylated linker region ...." in claims 1 and 2). None of the references cited teaches or suggests any antibody capable of selectively recognizing only Smad's that are phosphorylated at the linker region, because the conventional antibodies just recognize the phosphorylation itself and cannot distinguish between the phosphorylation of the C-terminal region and that of the linker region. The present polyclonal antibody can specifically recognize the phosphorylation of the linker region and consequently can be useful for selectively detecting diseases pathologically associated with the phosphorylation of the linker region.

Where an antigen is known, general technology for obtaining monoclonal antibodies as well as polyclonal antibodies to such an antigen has been established in the art. However, where there are a great number of antigenic candidates, there would be as well a great number of possible choices as to which antigen is selected to obtain the desired antibody. Such a choice is not obvious and rather difficult if no suggestion is provided. Accordingly, it is not obvious even to one of ordinary

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skill in the art to obtain an antibody capable of recognizing only Smad proteins which are phosphorylated at the linker region.

The importance of the phosphorylation of the linker region was not recognized before filing of the above-identified application. Under the circumstances, the present inventors found that the phosphorylation of the linker region is increased with the development of hepatic fibrosis and canceration and consequently associated with the hepatic fibrosis and canceration. Based on this finding, the present inventors found for the first time the fact that only the phosphorylation of the linker region is significant for the detection of those diseases.

Reconsideration of the rejection is therefore respectfully requested.

**Claims 3, 13 and 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.** (Office action paragraph no. 10)

Applicant has not amended claims 3, 13 and 14 to be independent at this time. Reconsideration of the objection to these claims is respectfully requested in view of the above arguments concerning the rejection of base claim 2.

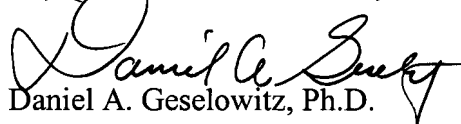
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If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact the Applicant's undersigned agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, the Applicant respectfully petitions for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

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